An Efficient Total Synthesis of (+)-Goniodiol

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Abstract: An efficient total synthesis of (+)-goniodiol was illustrated by using Carreira alkynylation and Sharpless asymmetric dihydroxylation as key steps.

Key words: styryl lactones, goniodiol, Carreira alkynylation, Sharpless asymmetric dihydroxylation

Styryl lactones are a series of natural products, exhibiting moderate to significant biological activity including antitumor and antifungal properties, as well as antibiotic potential.[1] Up to now, more than twenty styryl lactones have been isolated from plants and fungi.[2] (+)-Goniodiol (**1**) (Figure 1), an oxygenated 6-dihydrostyryl-5,6-dihydro-2-pyrone, was isolated from the leaves and twigs of *Goniothalamus sesquipedalis* (Annonaceae)[2c] and the stem bark of Thai *Goniothalamus giganteus*.[2d] Goniodiol exhibited potent selective cytotoxicity against human lung carcinoma cell lines A-549,[3] HL-60 cells,[4] and P-388 murine leukemia cells.[5]

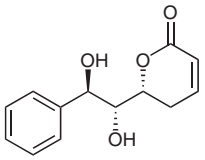


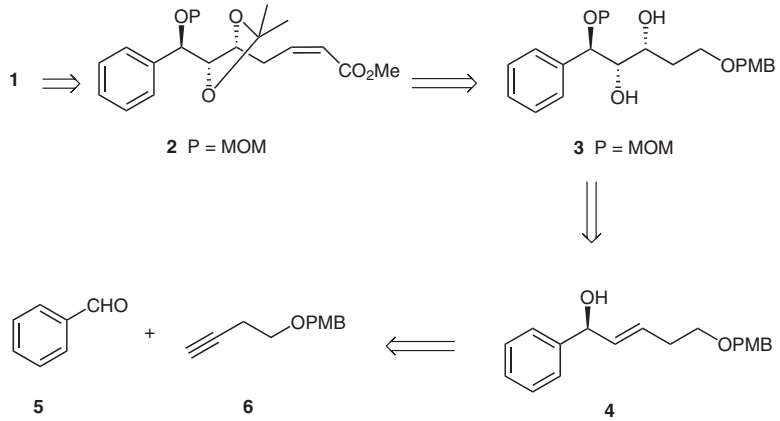
Figure 1 Structure of (+)-goniodiol (**1**)

Because of its unique and intriguing structure as well as antitumor activities, much efforts have been centered on the development of methodology for the synthesis of this molecule.[6,7] The majority of these syntheses utilize either chiral pool starting materials or enzymatic resolutions or longer reaction sequences.

In continuation of our interest in the synthesis of bioactive lactones,[8] we herein report a convenient synthesis of (+)-goniodiol (**1**) by utilizing Carreira alkynylation and Sharpless dihydroxylation reactions.

In our retrosynthetic analysis (Scheme 1), we envisaged that the target molecule **1** could be prepared through acid-catalyzed cyclization of compound **2**, which was obtained from *syn*-diol **3**. Compound **3** can be prepared from allylic alcohol **4**, which in turn could be easily derived from benzaldehyde **5** and the protected homopropargylic alcohol **6**.

The synthesis of (+)-goniodiol (**1**) (Scheme 2) commenced with the Carreira alkynylation reaction of benzaldehyde **5** with *p*-methoxybenzyl ether of homopropargylic alcohol **6** in the presence of (+)-*N*-methylephedrine, zinc triflate, and triethylamine[9] to afford the chiral propargylic alcohol **7** in 88% yield with high enantioselectivity. On the other hand, compound **7** can be prepared by an alternative route by the following reaction manipulations. Accordingly, benzaldehyde **5** was treated with PMB ether of homopropargylic alcohol **6** in presence of LHMDS to afford compound **8**, which on oxidition[10] with IBX in DMSO–CH_2Cl_2 afforded the corresponding ke-



Scheme 1 Retrosynthetic analysis of (+)-goniodiol (**1**)

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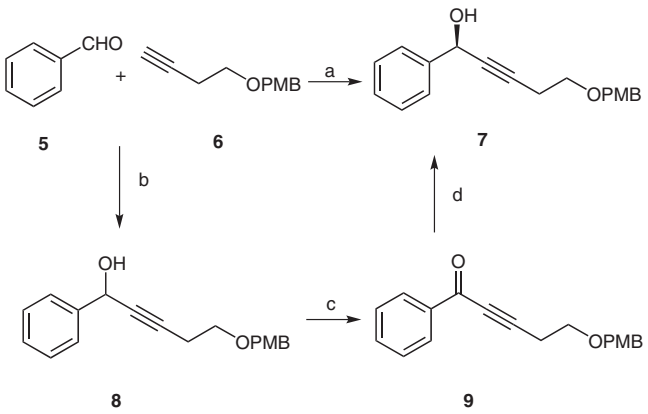
tone **9**. Now, ketone **9** on asymmetric reduction[11] with (*R*)-(Me)-CBS [(*R*)-2-methyl-CBS-oxazaborolidine] catalyst in the presence of $BH_3{\cdot}SMe_2$ gave the chiral propargylic alcohol **7** in 66% yield with excellent ee (Scheme 2).

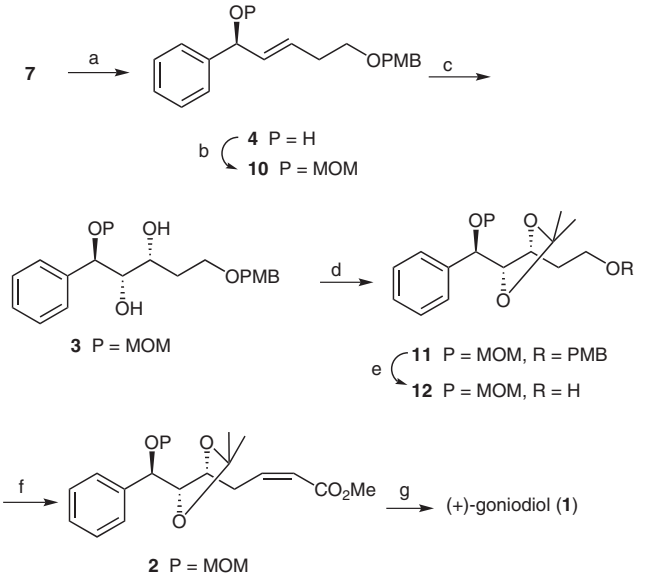


Scheme 2 *Reagents and conditions*: a) (+)-*N*-methylephedrine, $Zn(OTf)_2$, Et_3N, **6**, 2 h; then **5**, 1 h, r.t., 88% (90% ee); b) **6**, LHMDS, THF, 0 °C, 1 h, **5**, –78 to 25 °C, 2 h, 90%; c) IBX, DMSO, CH_2Cl_2, 0–25 °C, 92% d) (*R*)-(Me)-CBS, $BH_3{\cdot}SMe_2$, THF, –20 °C, 1 h, 66% (99% ee).

Compound **7** was reduced[12] with $LiAlH_4$ in THF to furnish the *E*-allylic alcohol **4**. The secondary hydroxy group of compound **4** was protected as its MOM ether[13] **10** by treating with MOM-Cl in the presence of Hünig's base in 92% yield. Compound **10** was then converted to *syn*-diol **3** by employing Sharpless asymmetric dihydroxylation conditions.[14] Thus, compound **10** was treated with AD-mix-β in *t*-BuOH–H_2O (1:1) to afford diol **3** as a single isomer in 90% yield, whereas on oxidative osmylation, compound **10** gave the desired compound **3** in 4:1 dr (94% yield). Subsequent acetonide protection[15] of hydroxy groups followed by the deprotection of PMB group[16] with H_2 over Pd/C furnished **12** in 96% yield (Scheme 3).

Oxidation[17] of alcohol **12** to its corresponding aldehyde and subsequent chain elongation[18] with Still–Gennari reagent furnished the *Z*-isomer **2** in 82% yield along with traces of *E*-isomer. Compound **2** on treating with catalytic amount of PTSA in EtOH at 50 °C afforded the target molecule **1** by tandem deprotection and in situ cyclization process. Spectral and analytical data of compound **1** were in agreement with the natural product.[3]

In summary, the total synthesis of (+)-goniodiol (**1**), a cytotoxic styryl lactone was accomplished in a stereocontrolled manner by the creation of chiral centers via Carreira alkynylation or CBS-reduction and Sharpless asymmetric dihydroxylation reactions in good overall yield.



Scheme 3 *Reagents and conditions*: a) $LiAlH_4$, THF, 0–25 °C, 3 h, 90%; b) MOM-Cl, DIPEA, CH_2Cl_2, 0–25 °C, 3 h, 96%; c) AD-mix-β, methanesulfonamide, *t*-BuOH–H_2O (1:1), 0 °C, 10 h, 90%; d) 2-methoxypropene, CSA, CH_2Cl_2, 0 °C, 10 min, 99%; e) H_2, 10% Pd/C, EtOAc–EtOH (1:1), 6 h, 25 °C, 96%; f) i. DMP, $NaHCO_3$, CH_2Cl_2, 0 °C, 30 min; ii) $MeO_2CCH_2P(O)(OCH_2CF_3)_2$, NaH, THF, 18-Crown-6, –78 °C, 1 h, 82%; g) *p*-TsOH, EtOH, 50 °C, overnight, 84%.

Reactions were conducted under N_2 in anhyd solvents such as CH_2Cl_2, THF, and EtOAc. All reactions were monitored by TLC (silica-coated plates and visualizing under UV light). Hexanes used refer to the fraction boiling in the range of 60 to 80 °C. Yields refer to chromatographically and spectroscopically (^1H and ^{13}C NMR) homogeneous material. Air sensitive reagents were transferred by syringe or cannula. Evaporation of solvents was performed at reduced pressure on a Büchi rotary evaporator. ^1H and ^{13}C NMR spectra of samples in $CDCl_3$ were recorded on Varian FT-400MHz and Bruker UXNMR FT-300 MHz (Avance) spectrometers. Chemical shifts are reported in δ relative to TMS (δ = 0.0) as an internal standard. Mass spectra were recorded E1 conditions at 70 eV on ES-MSD (Agilent technologies) spectrometers. Column chromatography was performed on silica gel (60–120 mesh) supplied by Acme Chemical Co., India. TLC was performed on Merck 60 F-254 silica gel plates. Optical rotations were measured with Jasco DIP-370 Polarimeter.

5-[(4-Methoxybenzyl)oxy]-1-phenylpent-2-yn-1-ol (8)

To a stirred solution of **6** (2.68 g, 14.13 mmol) in anhyd THF (15 mL) was added LHMDS (1 M solution in heptane, 23.5 mL, 23.55 mmol) at 0 °C under N_2 atmosphere. The reaction mixture was stirred at the same temperature for 1 h and cooled to –78 °C. Then **5** (1.0 g, 9.42 mmol) was added slowly via a syringe and the mixture was allowed to warm to 25 °C. After completion of the reaction (as indicated by TLC), the mixture was quenched with sat. aq NH_4Cl (10 mL) and diluted with EtOAc (20 mL). The mixture was extracted with EtOAc (2 × 10 mL), and the combined organic layers were washed with brine (2 × 20 mL) and H_2O (2 × 20 mL), and dried (Na_2SO_4). Concentration under vacuum gave the crude product, which was purified by column chromatography using 20% EtOAc in hexanes to afford **8** as a pale yellow oil; yield: 2.51 g (90%).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 7.0 Hz, 2 H), 7.35–7.27 (m, 3 H), 7.20 (d, *J* = 8.6 Hz, 2 H), 6.80 (d, *J* = 8.6 Hz, 2 H), 5.38 (d, *J* = 5.8 Hz, 1 H), 4.45 (s, 2 H), 3.79 (s, 3 H), 3.55 (t, *J* = 6.5 Hz, 2 H), 2.55 (dt, *J* = 6.6, 2.2 Hz, 2 H).

ESMS: *m*/*z* = 319 $[M + Na]^+$.

5-[(4-Methoxybenzyl)oxy]-1-phenylpent-2-yn-1-one (9)

To an ice-cold solution of IBX (0.9 g, 3.24 mmol) in DMSO (2.0 mL), was added a solution of **8** (0.8 g, 2.70 mmol) in anhyd CH_2Cl_2

(5 mL) and the reaction mixture was stirred at 25 °C for 3 h. The mixture was diluted with CH_2Cl_2 (20 mL), filtered through a Celite pad, and the pad was washed with CH_2Cl_2 (3 × 10 mL). The combined filtrates were washed with H_2O (2 × 10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The resultant residue was purified by column chromatography using 12% EtOAc in hexanes to afford ketone **9** as a pale yellow oil; yield: 0.73 g (92%).

IR (neat): 2927, 2863, 2237, 1643, 1256, 1095 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.10 (dd, *J* = 7.1, 1.3 Hz, 2 H), 7.55 (tt, *J* = 7.3, 1.3 Hz, 1 H), 7.41 (t, *J* = 7.1 Hz, 2 H), 7.23 (d, *J* = 8.5 Hz, 2 H), 6.82 (d, *J* = 8.5 Hz, 2 H), 4.49 (s, 2 H), 3.78 (s, 3 H), 3.67 (t, *J* = 6.8 Hz, 2 H), 2.75 (t, *J* = 6.8 Hz, 2 H).

ESMS: *m*/*z* = 317 $[M + Na]^+$.

(1*S*)-5-[(4-Methoxybenzyl)oxy]-1-phenylpent-2-yn-1-ol (7)

Procedure A: A 1 M solution of (*R*)-(Me)-CBS in toluene (0.40 mL, 0.40 mmol) under static atmosphere of N_2 was dissolved in anhyd THF (5 mL). To this solution was added $BH_3{\cdot}SMe_2$ (0.20 mL, 2.04 mmol) and the mixture was cooled to –20 °C. Prochiral ketone **9** (0.6 g, 2.04 mmol), either neat or concentrated solution in THF, was added via a syringe and the mixture was stirred at –20 °C for 1 h. The reaction was quenched with MeOH (0.5 mL) at the same temperature, then allowed to warm to 25 °C. The solvent was removed under reduced pressure and the residue was purified by column chromatography using 15% EtOAc in hexanes to afford the pure alcohol **7** as a pale yellow oil; yield: 0.40 g (66%, 99% ee).

Procedure B: (+)-*N*-Methylephedrine (0.25 g, 1.41 mmol) and $Zn(OTf)_2$ (0.51 g, 1.41 mmol) were dried at 120 °C under vacuum, then flushed with N_2 gas for 15 min. To the mixture was added Et_3N (0.2 mL, 1.41 mmol), PMB ether of homopropargyl alcohol **6** (0.26 g, 1.41 mmol), either neat or at very high concentration in toluene, and the resultant mixture was stirred for 2 h. Then benzaldehyde **5** (0.1 g, 0.94 mmol) was added dropwise slowly. The reaction mixture was stirred for 1 h, quenched with aq NH_4Cl (10 mL), and diluted with Et_2O (30 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under vacuum. The residue was purified by silica gel column chromatography using 15% EtOAc in hexanes to afford the propargyl alcohol **7**; yield: 0.53 g (88%, 90% ee) as a pale yellow oil; $[\alpha]_D^{25}$ +5.3 (*c* 2.0, $CHCl_3$).

IR (neat): 3418, 3029, 2921, 2864, 2233, 1249, 1093 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 7.3 Hz, 2 H), 7.35–7.27 (m, 3 H), 7.20 (d, *J* = 8.8 Hz, 2 H), 6.80 (d, *J* = 8.8 Hz, 2 H), 5.38 (d, *J* = 5.8 Hz, 1 H), 4.45 (s, 2 H), 3.79 (s, 3 H), 3.55 (t, *J* = 6.6 Hz, 2 H), 2.55 (dt, *J* = 6.6, 2.2 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.0, 141.0, 129.8, 129.2, 128.3, 128.0, 126.5, 113.7, 83.8, 81.2, 72.4, 67.7, 64.4, 55.1, 20.1.

ESMS: *m*/*z* = 319 $[M + Na]^+$.

(1*S*,2*E*)-5-[(4-Methoxybenzyl)oxy]-1-phenylpent-2-en-1-ol (4)

To a stirred suspension of $LiAlH_4$ (0.10 g, 2.13 mmol) in THF (5 mL) at 0 °C was added dropwise a solution of compound **7** (0.5 g, 1.77 mmol) in THF (15 mL). The reaction mixture was allowed to attain 25 °C and stirred for 4 h. It was then cooled to 0 °C, diluted with Et_2O (30 mL), and quenched by dropwise addition of sat. aq NH_4Cl (2 mL). The solid material was filtered and washed thoroughly with hot EtOAc for several times. The combined organic layers were washed with H_2O (15 mL) and brine (10 mL), and dried (Na_2SO_4). The organic layer was concentrated under reduced pressure and the residue was purified by column chromatography using 15% EtOAc in hexanes to afford compound **4** as a colorless liquid; yield: 0.45 g (90%); $[\alpha]_D^{25}$ –5.7 (*c* 1.0, $CHCl_3$).

IR (neat): 2928, 2858, 1464, 1104, 1040, 838, 777 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.28 (m, 5 H), 7.17 (d, *J* = 8.6 Hz, 2 H), 6.80 (d, *J* = 8.6 Hz, 2 H), 5.73–5.68 (m, 2 H), 5.11 (dd, *J* = 4.9, 2.0 Hz, 1 H), 4.39 (s, 2 H), 3.79 (s, 3 H), 3.45 (t, *J* = 6.6 Hz, 2 H), 2.37–2.30 (m, 2 H).

ESMS: *m*/*z* = 321 $[M + Na]^+$.

1-Methoxy-4-{[(*E*,5*S*)-5-(methoxymethoxy)-5-phenylpent-3-enyl]oxymethyl}benzene (10)

To a stirred solution of compound **4** (0.3 g, 1.00 mmol) in CH_2Cl_2 (10 mL) at 0 °C under N_2 atmosphere was added *i*-Pr_2NEt (Hünig's base) (0.51 mL, 3.02 mmol), and after 5 min MOMCl (0.13 mL, 1.50 mmol) was added dropwise. After stirring for 3 h at 25 °C, the reaction mixture was diluted with CH_2Cl_2 (20 mL). The combined organic layers were washed with sat. aq NH_4Cl (2 × 5 mL), brine (2 × 5 mL) and H_2O (1 × 5 mL), and dried (Na_2SO_4). The solvent was removed under vacuum and the residue was purified on a silica gel column using 10% EtOAc in hexanes to afford the pure compound **10** as a pale yellow liquid; yield: 0.33 g (96%); $[\alpha]_D^{25}$ +0.3 (*c* 1.5, $CHCl_3$).

IR (neat): 3029, 2938, 2864, 1606 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.24 (m, 5 H), 7.12 (d, *J* = 8.3 Hz, 2 H), 6.75 (d, *J* = 8.3 Hz, 2 H), 5.73–5.49 (m, 2 H), 4.96 (d, *J* = 6.8 Hz, 1 H), 4.63 (d, *J* = 6.8 Hz, 1 H), 4.48 (d, *J* = 6.8 Hz, 1 H), 4.34 (s, 2 H), 3.74 (s, 3 H), 3.41 (t, *J* = 6.8 Hz, 2 H), 3.30 (s, 3 H), 2.34–2.26 (m, 2 H).

ESMS: *m*/*z* = 365 $[M + Na]^+$.

(1*R*,2*S*,3*R*)-5-[(4-Methoxybenzyl)oxy]-1-(methoxymethoxy)-1-phenylpentane-2,3-diol (3)

A 50 mL round-bottomed flask, equipped with a magnetic stirrer, is charged with *t*-BuOH (6 mL), H_2O (6 mL), 1.79 g of AD-mix-β (1.28 mmol), and $MeSO_2NH_2$ (125 mg, 1.17 mmol). The mixture was stirred at 25 °C until both phases were clear and then cooled to 0 °C, whereupon the inorganic salts partially precipitated. Then olefin **10** (400 mg, 1.17 mmol) was added at once, and the heterogeneous slurry was stirred vigorously at 0 °C until TLC revealed the absence of the starting olefin (10 h). The reaction was quenched at 0 °C by the addition of Na_2SO_3 (500 mg) and then warmed to 25 °C and stirred for 30–60 min. The mixture was extracted several times with CH_2Cl_2, the combined organic layers were washed with aq 2 N KOH (5 mL), and dried ($MgSO_4$). Removal of the solvent gave the crude compound, which on purification by flash chromatography (silica gel, 50% EtOAc in hexanes) afforded the pure diol **3** as a pale yellow oil; yield: 0.39 g (90%); $[\alpha]_D^{25}$ –86.0 (*c* 1.0, $CHCl_3$).

IR (neat): 3451, 2930, 1611, 1247, 1097 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.31 (m, 5 H), 7.16 (d, *J* = 8.3 Hz, 2 H), 6.81 (d, *J* = 8.3 Hz, 2 H), 4.67 (d, *J* = 6.8 Hz, 1 H), 4.53 (ABq, *J* = 6.8 Hz, 2 H), 4.40 (s, 2 H), 4.41–4.05 (m, 2 H), 3.79 (s, 3 H), 3.60 (t, *J* = 5.2 Hz, 2 H), 3.54–3.48 (m, 1 H), 3.34 (s, 3 H), 2.99 (d, *J* = 4.5 Hz, 1 H), 2.47 (d, *J* = 6.8 Hz, 1 H), 2.00–1.82 (m, 1 H), 1.79–1.67 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 138.8, 130.0, 129.2, 128.3, 128.0, 127.6, 113.7, 94.6, 79.0, 76.0, 72.8, 68.3, 67.4, 55.2, 33.6.

ESMS: *m*/*z* = 399 $[M + Na]^+$.

(4*R*,5*R*)-4-{2-[(4-Methoxybenzyl)oxy]ethyl}-5-[(*R*)-(methoxymethoxy)(phenyl)methyl]-2,2-dimethyl-1,3-dioxolane (11)

Catalytic amount of CSA was added to a stirred solution of diol **3** (1.1 g, 2.90 mmol) and 2-methoxypropene (0.42 g, 4.40 mmol) in CH_2Cl_2 (10 mL) at 0 °C and the reaction mixture was allowed to stir for 10 min. The mixture was quenched with Et_3N (0.2 mL) and the solvent was removed under vacuum. The crude product was purified by column chromatography using 5% EtOAc in hexanes to af-

ford the pure product **11** as a colorless oil; yield: 1.20 g (99%); $[\alpha]_D^{25}$ –63.5 (*c* 1.0, $CHCl_3$).

IR (neat): 2928, 2846, 1248, 1029 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.26 (m, 5 H), 7.20 (d, *J* = 9.0 Hz, 2 H), 6.81 (d, *J* = 9.0 Hz, 2 H), 4.64 (d, *J* = 6.0 Hz, 1 H), 4.50 (s, 2 H), 4.39 (s, 2 H), 4.08 (dt, *J* = 8.3, 3.0 Hz, 1 H), 3.85 (dt, *J* = 7.5, 6.0 Hz, 1 H), 3.79 (s, 3 H), 3.55–3.50 (m, 2 H), 3.30 (s, 3 H), 1.90–1.79 (m, 1 H), 1.75–1.62 (m, 1 H), 1.32 (s, 3 H), 1.26 (s, 3 H).

LCMS: *m*/*z* = 439 $[M + Na]^+$.

2-{(4*R*,5*R*)-5-[(*R*)-(Methoxymethoxy)(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}ethan-1-ol (12)

Catalytic amount of 10% Pd/C was added to a solution of compound **11** (0.6 g, 1.44 mmol) in EtOAc (2 mL) and EtOH (2 mL) and the mixture was stirred for 6 h at 25 °C under H_2 atm. After completion of the reaction, the reaction mixture was filtered through a Celite pad and washed with EtOAc (2 × 10 mL). The solvent was removed under vacuum and the crude product was subjected to flash column chromatography (eluent: 35% EtOAc in hexanes) to furnish the pure alcohol **12**; yield 0.40 g (96%).

IR (neat): 3446, 2932, 1030, 703 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.28 (m, 5 H), 4.68 (d, *J* = 6.0 Hz, 1 H), 4.53 (ABq, *J* = 6.7 Hz, 2 H), 4.21–4.13 (m, 1 H), 3.89 (dd, *J* = 7.5, 6.0 Hz, 1 H), 3.71 (t, *J* = 4.5 Hz, 2 H), 3.34 (s, 3 H), 2.26 (br s, 1 H), 1.72–1.64 (m, 2 H), 1.35 (s, 3 H), 1.34 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.6, 128.4, 128.2, 127.8, 109.0, 94.2, 83.5, 77.6, 60.2, 60.1, 56.9, 36.4, 27.3, 26.9.

ESMS: *m*/*z* = 319 $[M + Na]^+$.

Methyl (*Z*)-4-{(4*R*,5*R*)-5-[(*R*)-(Methoxymethoxy)(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}but-2-enoate (2)

Dess–Martin periodinane (515 mg, 1.21 mmol) was added to a stirred solution of primary alcohol **12** (300 mg, 1.01 mmol) and $NaHCO_3$ (127 mg, 1.52 mmol) in CH_2Cl_2 (15 mL) at 0 °C and the reaction mixture was stirred for 30 min. After completion of the reaction, the mixture was diluted with CH_2Cl_2 (15 mL). The combined organic layers were washed with H_2O (15 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was subjected to *cis*-olefination without further purification. Thus, a solution of bis(trifluoromethanephosphono) acetate (354 mg, 1.11 mmol) in THF (5 mL) was added to a suspension of NaH (29 mg, 1.21 mmol) and a catalytic amount of 18-Crown-6 in THF (5 mL) at 0 °C. The mixture was stirred for 30 min, then it was cooled to –78 °C and treated with a solution of crude aldehyde obtained as above in THF (5 mL). After completion of the reaction, the excess NaH was quenched by the dropwise addition of aq NH_4Cl (10 mL) and extracted with Et_2O (2 × 10 mL). The combined organic layers were washed with H_2O (10 mL), dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography using 5% EtOAc in hexanes to furnish the pure *cis*-olefin **2**; yield: 0.5 g (82%).

IR (neat): 2924, 2853, 1722, 1646, 1024, 703 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.29 (m, 5 H), 6.31 (td, *J* = 12.3, 6.8 Hz, 1 H), 5.82 (td, *J* = 11.3, 2.2 Hz, 1 H), 4.65 (d, *J* = 6.0 Hz, 1 H), 4.53 (ABq, *J* = 6.8 Hz, 2 H), 4.02 (dt, *J* = 7.5, 3.7 Hz, 1 H), 3.88 (dd, *J* = 7.5, 6.0 Hz, 1 H), 3.69 (s, 3 H), 3.33 (s, 3 H), 3.03–2.92 (m, 1 H), 2.88–2.77 (m, 1 H), 1.35 (s, 3 H), 1.28 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 145.3, 137.6, 128.2, 128.1, 128.0, 120.9, 109.2, 94.2, 82.9, 77.6, 74.4, 55.8, 51.0, 32.8, 27.3, 26.8.

ESMS: *m*/*z* = 373 $[M + Na]^+$.

(6*R*)-6-[(1*R*,2*R*)-1,2-Dihydroxy-2-phenylethyl]-5,6-dihydro-2*H*-pyran-2-one [(+)-Goniodiol, 1]

Catalytic amount of PTSA was added to a solution of compound **2** (0.3 g, 0.85 mmol) in EtOH (10 mL). The reaction mixture was stirred overnight at 50 °C. After completion of the reaction, the mixture was quenched with sat. aq $NaHCO_3$ (0.2 mL), and the solvent was removed under vacuum. The crude residue was purified to afford the target molecule **1**; yield: 0.17 g (84%); $[\alpha]_D^{25}$ +72.8 (*c* 1.0, $CHCl_3$).

IR (neat): 3405, 2923, 2853, 1706 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.33 (m, 5 H), 6.90 (ddd, *J* = 9.5, 6.5, 2.2 Hz, 1 H), 5.98 (dd, *J* = 9.5, 2.9 Hz, 1 H), 4.93 (d, *J* = 6.5 Hz, 1 H), 4.74 (td, *J* = 13.1, 2.9 Hz, 1 H), 3.71–3.66 (m, 1 H), 2.84–2.74 (m, 1 H), 2.39–2.27 (m, 1 H), 2.18–2.09 (m, 1 H), 2.06–1.97 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.3, 145.8, 140.0, 128.7, 128.3, 126.5, 120.8, 75.1, 73.8, 29.7.

ESMS: *m*/*z* = 257 $[M + Na]^+$.

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References

(1) (a) Mu, Q.; Tang, W. D.; Liu, R. Y.; Li, C. M.; Lou, L. G.; Sun, H. D. *Planta Med.* **2003**, *69*, 826. (b) Pihie, A. H.; Stanslas, J.; Din, L. B. *Anticancer Res.* **1998**, *18*, 1739.

(2) (a) Wu, Y. C.; Duh, C. Y.; Chang, F. R.; Wang, S. K.; Chang, J. J.; McPhail, D. R.; McPhail, A. T.; Lee, K. H. *J. Nat. Prod.* **1991**, *54*, 1077. (b) Sam, T. W.; Saw-Yeu, C.; Matsjeh, S.; Gan, E. K.; Razak, D.; Mohamed, A. L. *Tetrahedron Lett.* **1987**, *28*, 2541. (c) Talapatra, S. K.; Basu, D.; Goaswami, S.; Talapatra, B. *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1985**, *24*, 29. (d) Alkofahi, A.; Ma, W. W.; Mckenze, A. T.; Byrn, S. R.; Mclaughlin, J. L. *J. Nat. Prod.* **1989**, *52*, 1371. (e) Fang, X. P.; Anderson, J. E.; Qui, X. X.; Kozlowski, J. F.; Mclaughlin, J. L. *Tetrahedron* **1993**, *49*, 1563.

(3) Fang, X. P.; Anderson, J. E.; Chang, C. J.; Mclaughlin, J. L.; Fanwick, P. E. *J. Nat. Prod.* **1991**, *54*, 1034.

(4) Nakashima, K.; Kikuchi, N.; Shirayama, D.; Miki, T.; Ando, K.; Sono, M.; Suzuki, S.; Kawasw, M.; Kondoh, M.; Sato, M.; Kanai, K.; Nagase, H.; Honda, T. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 387.

(5) Tsubuki, M.; Kanai, K.; Nagase, H.; Honda, T. *Tetrahedron* **1999**, *55*, 2493.

(6) (a) Tsubiki, M.; Kanai, K.; Honda, T. *J. Chem. Soc., Chem. Commun.* **1992**, 1640. (b) Annaick, F.; Francois, C.; Michael, D.; Bertrand, C. *Eur. J. Org. Chem.* **2008**, *29*, 4900. (c) Mukai, C.; Hirai, S.; Hanaoka, M. *J. Org. Chem.* **1997**, *62*, 6619. (d) Surivet, J. P.; Goré, J.; Vatèle, J. M. *Tetrahedron* **1996**, *37*, 14877. (e) Prasad, K. R.; Gholap, S. L. *Tetrahedron Lett.* **2007**, *48*, 4679. (f) Tsubuki, M.; Kanai, K.; Nagase, H.; Honda, T. *Tetrahedron* **1999**, *55*, 2493. (g) Surivet, J. P.; Vetele, J. M. *Tetrahedron Lett.* **1998**, *39*, 7299. (h) Edward, T. W.; Darren, D. J.; Steven, L. V. *Org. Biomol. Chem.* **2006**, *4*, 1698. (i) Ramachandran, P. V.; Subash, C. J.; Reddy, M. V. *J. Org. Chem.* **2002**, *67*, 7547.

(7) (a) Chen, J.; Lin, G.-Q.; Wang, Z.-M.; Liu, H.-Q. *Synlett* **2002**, 1265. (b) Banwell, M. G.; Coster, M. J.; Karunaratne, O. P.; Smith, J. A. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1622. (c) Yadav, J. S.; Krishna, V. H.; Srilatha, A.; Somaiah, R.; Reddy, B. V. *Synthesis* **2010**, 3004. (d) Yadav, J. S.; Premalatha, K.; Harshavardhan, S.; Reddy, B. V. *Tetrahedron Lett.* **2008**, *49*, 6765.
(8) (a) Sabitha, G.; Sudhakar, K.; Yadav, J. S. *Synthesis* **2007**, 385. (b) Sabitha, G.; Narjis, F.; Gopal, P.; Reddy, C. N.; Yadav, J. S. *Tetrahedron: Asymmetry* **2009**, *20*, 184. (c) Sabitha, G.; Prasad, M. N.; Shankaraiah, K. S.; Jadav, J. S. *Synthesis* **2010**, 1171. (d) Sabitha, G.; Bhaskar, V.; Reddy, S. S. S.; Yadav, J. S. *Helv. Chim. Acta* **2010**, *93*, 329.
(9) (a) Boyall, D.; Frantz, D. E.; Carreira, E. M. *Org. Lett.* **2002**, *4*, 2605. (b) Fettes, A.; Carreira, E. M. *J. Org. Chem.* **2003**, *68*, 9274.
(10) Serrat, X.; Cabarrocas, G.; Ventura, M.; Linden, A.; Villalgordo, J. M. *Tetrahedron: Asymmetry* **1999**, *10*, 3417.
(11) (a) Wendt, K. U.; Schulz, G. E.; Liu, D. R.; Corey, E. J. *Angew. Chem. Int. Ed.* **2000**, *39*, 2812. (b) Corey, E. J.; Shibata, S.; Bakshi, R. K. *J. Org. Chem.* **1988**, *53*, 2861. (c) Scheerer, J. R.; Lawrence, J. F.; Wang, G. C.; Evans, D. A. *J. Am. Chem. Soc.* **2007**, *129*, 8968.
(12) Yadav, J. S.; Bandhopadhayaya, A.; Kunwar, A. C. *Tetrahedron Lett.* **2001**, *42*, 4907.
(13) Li, L.-S.; Wu, Y.-L. *Tetrahedron* **2002**, *58*, 9049.
(14) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.
(15) Oikawa, Y.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron Lett.* **1982**, *23*, 889.
(16) Pang, J.-H.; Ham, Y.-J.; Lee, D.-H. *Bull. Korean Chem. Soc.* **2003**, *24*, 891.
(17) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **2004**, *69*, 2091.
(18) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.